## PEER REVIEW HISTORY



## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Changes in Self-Report Sexually Transmitted Infections among Married Couples in India from 2006 to 2016: A Repeated Cross-sectional Multivariate Analysis from Nationally Representative Data |
| **AUTHORS** | Choi, Jasmin; Bahl, Deepika; Arora, Monika; Xuan, Ziming |

## VERSION 1 – REVIEW

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| **REVIEWER** | Wand, Handan<br>The Kirby Institute for Infection and Immunity in Society, University of New South Wales |
| **REVIEW RETURNED** | 05-Apr-2021 |

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| **GENERAL COMMENTS** | This paper investigates trends in sexually transmitted infections among married couples in India.<br>Overall, this is a well-written paper. I have only minor comments:<br><br>#1: Do married couples imply that the couples are cohabiting as well? It is very important to distinguish between married/cohabiting couples vs. married but not cohabiting.<br>#2: Although the study use the terminology “trend”, the data at hand is limited to only two time points. This is a major limitations of the study. In addition to this, there is a “decade” long gap between these 2 time points. That would be informative to compare the results with other studies conducted during this period. What has changed? Why? How? Otherwise it is too strong to call the study and titled it as “trend” |

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| **REVIEWER** | Lonnee-Hoffman , Risa Anna Margareth<br>NTNU |
| **REVIEW RETURNED** | 07-May-2021 |

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| **GENERAL COMMENTS** | First of all, thank you for performing this interesting analysis, which will be able to add valuable information to the existing knowledge on the dynamics of particular STI symptoms and other genital symptoms in India. However, according to my review of the manuscript, some important considerations and changes need to be made. I will address the issues according to the points marked as " no" above.<br>3. The study design is in my opinion not appropriate to assess the research question: To measure STIs, it is not sufficient to analyze self reported symptoms. STI symptoms are only present in less than half of all cases. In particular the symptoms of unpleasant smelling vaginal discharge, is in most cases not associated with STIs and due to bacterial vaginosis. Hence, very low sensitivity and specificity for these self-reported symptoms for STIs.<br>However, the outcomes are interesting, but the research question needs be formulated accordingly This should be reflected in the title.<br>4. The methods are described insufficiently. You need to report more details on the population included- and particularly on the ones not responding and what is done with missing data. A flow chart could be helpful.<br>6. The outcome is not appropriately described: |

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| | You need to present demographics inclusive social background of the included population more clearly.<br>Please describe the difference between sores and ulcers.<br>9. This is affected by the same problems as point 3.<br>10. The results are not described clearly. Tables only containing odds ratios and CI are not showing the whole picture. In the tables, absolute numbers and proportions need to be presented.<br>Can you elaborate more why you describe group prevalence of STIs, when one of the partners is positive? Again, we also need to know more about the included individuals vs couples.<br>How is it possible that numbers for "casts" are too low to report with such a large number of included people? Again, demographics and missing numbers would be very interesting in this context.<br><br>Further: The sentence page 7 line 23-25 is unclear.<br>Also page 7 line 36-37: is this a correct statement?<br>Page 7 line 32-34: a decrease in the use of health care facilities does not automatically mean the use is minimal. Be precise and the absolute numbers and proportions need to be presented.<br>Reference 6 is seems to be outdated (global epidemic of STD from 1998)<br><br>With sincere regards and good luck. |

**VERSION 1 – AUTHOR RESPONSE**

| **Reviewer: 1**<br>Dr. Handan Wand, The Kirby Institute for Infection and Immunity in Society | |
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| **Comments to the Author:** | **Authors' Responses:** |
| This paper investigates trends in sexually transmitted infections among married couples in India.<br>Overall, this is a well-written paper. I have only minor comments: | We want to thank reviewer's overall favorable assessment. |
| #1: Do married couples imply that the couples are cohabiting as well? It is very important to distinguish between married/cohabiting couples vs. married but not cohabiting. | Thank you for raising this question. The rates of females who do not currently reside with their husband at the time of the survey was 0.37% for 2016 and 0.62% for 2006. The rates of males who do not currently reside with their wife at the time of the survey was 0.14% for 2016 and 0.26% for 2006. We described this distinction in the revision (line 44-46, pg 2) and wish to note that the proportions of partner not cohabitating at the time of the survey were less than 1%, which is too small to change the results of the study. |
| #2: Although the study use the terminology "trend", the data at hand is limited to only two time points. This is a major limitations of the study. In addition to this, there is a "decade" long gap between these 2 time points. That would be informative to compare the results with other studies conducted during this period. What has changed? Why? How? Otherwise it is too strong to call the study and titled it as "trend" | We rephrased the title to reflect the data more accurately. Unfortunately, as noted in the manuscript, we could not identify any other comparative studies at national level that contain STI information.<br><br>We updated the Discussion section to acknowledge the limitation of having only two time points with a large time gap (line 16-17, pg 7) |
| **Reviewer: 2**<br>Dr. Risa Anna Margareth Lonnee-Hoffman , NTNU | |
| **Comments to the Author:** | **Authors' Responses:** |
| First of all, thank you for performing this interesting analysis, which will be able to add valuable information to the existing knowledge on the dynamics of particular STI symptoms and other genital symptoms in India. However, according to my review of the | We want to thank the reviewer's overall verdict on our manuscript. |

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| manuscript, some important considerations and changes need to be made. I will address the issues according to the points marked as " no" above [Editor note: the reviewers fill in a numbered checklist to indicate they have considered certain aspects in the review - the numbers of the comments correspond to the checklist]. | |
| 3. The study design is in my opinion not appropriate to assess the research question: To measure STIs, it is not sufficient to analyze self reported symptoms. STI symptoms are only present in less than half of all cases. In particular the symptoms of unpleasant smelling vaginal discharge, is in most cases not associated with STIs and due to bacterial vaginosis. Hence, very low sensitivity and specificity for these self-reported symptoms for STIs. However, the outcomes are interesting, but the research question needs be formulated accordingly<br><br>This should be reflected in the title. | We looked at STI status only (not symptoms) for Table 3 and Table 4 to assess the sociodemographic factors. The symptoms are taken into consideration for Table 5 when looking at whether they sought advice or treatment, since the survey questions are only asked to people who report STI status or symptoms.<br><br>We acknowledge the limitation of self-report data as it lack the diagnostic rigor compared to clinical data (line 8-12, pg 7). We wish to emphasize that this nationally representative data provides useful epidemiologic evidence that is typically not available in smaller clinical samples.<br><br>We rephrased the title to reflect the self-report nature of the collected data. |
| 4. The methods are described insufficiently. You need to report more details on the population included- and particularly on the ones not responding and what is done with missing data. A flow chart could be helpful. | Thank you for this feedback. Flow chart is included in the revision (Figure 1). We would like to note that the magnitude of missing data is rather minimal (around 5% for the multivariate analysis on STI and symptoms and less than 2% for advice/treatment analyses), so we excluded the missing cases and proceeded with complete-case analysis. |
| 6. The outcome is not appropriately described:<br>You need to present demographics inclusive social background of the included population more clearly.<br><br>Please describe the difference between sores and ulcers. | We updated the manuscript to provide background characteristics of married couple in a table format (Table 1). We provided a brief description of the demographics in the manuscript (line 9-13, pg 4).<br><br>We wish to note that the survey questionnaire does not distinguish between sores and ulcers. The question on the survey states: “Sometimes men have a sore or ulcer near their penis. During the last 12 months, have you had a sore or ulcer on or near your penis?” for men; “Sometimes women have a genital sore or ulcer. During the last 12 months, have you had a genital sore or ulcer?” for women. |
| 9. This is affected by the same problems as point 3 [Editor note: the reviewer means that the conclusions are not adequately supported by the data]. | Thank you for this feedback. As stated above, we would like to acknowledge the limitation of self-report data. We hope that our effort to address this concern by changing the title and elaborating further in the limitation section is sufficient to the reviewer. Again, we wish to emphasize the large scope of this epidemiological data can be useful as compared to smaller clinical sample. |
| 10. The results are not described clearly. Tables only containing odds ratios and CI are not showing the whole picture. In the tables, absolute numbers and proportions need to be presented.<br><br>Can you elaborate more why you describe group prevalence of STIs, when one of the partners is positive? Again, we also need to know more | Thank you for this feedback. We updated the n value and proportion of STI for Table 3.<br><br>Our rationale for using couple prevalence is that the trend across two waves remains similar for husband and wife. In Table 2, the husband’s and wife’s STIs all significantly increased from 2006 to 2016, which is consistent with couple’s STI prevalence. I believe it’s easier to digest as a reader to see one STI outcome at couple-level (instead of two individual levels of husband and wife) when looking at |

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| about the included individuals vs couples.<br><br>How is it possible that numbers for "casts" are too low to report with such a large number of included people? Again, demographics and missing numbers would be very interesting in this context. | the associations with SES factors. We also included this explanation in the manuscript (line 12-16, pg 3).<br><br>Among husbands who reported “don’t know” for their castes, there are 0 case of STI for husbands and 2 cases for wives. Among women who reported “don’t know” for their castes, there are 3 cases of STI for husbands and 6 cases for wives.<br>The zero count makes it difficult to assess in multivariate analyses. In models with interaction terms, which we included year as an indicator variable, the counts for certain categories in caste become too small as described above. Hence, we observed the unstable estimates in the caste variables in adjusted OR as a result of inflated standard error estimates.<br><br>In light of reviewer’s comment, we regrouped the caste categorization to count the people who did not know their castes as “others (none of them).” After we have done the regrouping, we ran the analyses again and updated the tables and manuscript accordingly (line 28-29, pg 3). We wish to note that the conclusion of the study remains the same after updating the results. |
| Further: The sentence page 7 line 23-25 is unclear. | We clarified the sentence by revising as following: “A combination of these two factors may have contributed to the higher rates of self-report STIs among the wealthier group. It is unclear that these changes in family dynamics may contribute to intimate partner relationships and subsequently affect sexual health among married couples.”<br> “Imbalance of wealth among husband and wife may contribute to shift of family dynamics that may further affect sexual health and broadly intimate partner relationship.”<br>(line 34-36, pg 6) |
| Also page 7 line 36-37: is this a correct statement? | Thank you for raising this question. We have deleted the sentence to avoid confusion. |
| Page 7 line 32-34: a decrease in the use of health care facilities does not automatically mean the use is minimal. Be precise and the absolute numbers and proportions need to be presented. | Thank you for this feedback. We revised the sentences to more accurately reflect our conclusion (line 42-46, pg 7). |
| Reference 6 is seems to be outdated (global epidemic of STD from 1998) | Thank you for bringing this to our attention. We updated the references. |

**VERSION 2 – REVIEW**

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| **REVIEWER** | Lonnee-Hoffman , Risa Anna Margareth<br>NTNU |
| **REVIEW RETURNED** | 20-Jun-2021 |

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| **GENERAL COMMENTS** | Dear Authors!<br>The manuscript is much improved, thank you for that. However, there are still some issues.<br>1. Most importantly, I cannot agree on your aim/objective for the study, given the available<br>outcome. Your outcomes are self- reported STIs and possible symptoms of STIs. There for this should be stated consistently without leading to misunderstandings.<br>2. See above. Therefore both objectives and results should be changed accordingly. |

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| | 3. The design is not possible to change. Therefore you should re-formulate the research question.<br>4. The inclusion criteria for the selected cohort are still not described, neither is the method of data collection described.<br>5. For the original data collection- was there no consent required? And, were the partners aware of each others answers?<br>6. The outcome measure of self reported STI and STI symptoms is appropriate. However, it is not quite clear and convincing why an artificial outcome needs to be constructed - the couples STI status. This outcome has not been measured directly and should be not used as a hard outcome in tables in line with collected data. Either a more convincing explanation of this construction should be given in the method section or it could be mentioned in the discussion as possible interpretation of the results.<br>The casts should be explained shortly in the method section, as this is not commonly known and one wonders, if there could be a more culturally sensitive term than"backward class".<br>The questions are not quite clear. Only when looking at the results, it becomes more clear, that seperate questions are asked. Was there a separate question on "any STI symptoms" or is this a constructed variable?<br>9 and 10. Some of this is already mentioned. The results should be still more clearly presented.<br>- Nearly 50% more women have a higher education in 2016 compared to 2006, although employment is much less. this should be mentioned when presenting the results. SE is not that interesting, it could be in brackets , not an own column. Rather a statistical difference could be considered to be presented. Further, in the discussion this should mentioned,and explanations offered- are different populations selected, has the social pattern changed...?<br>- Table 2: consider to have the year as column, the variables as rows. Recommend to drop "couples". It would be easier to read if the Chi - square is dropped and rather the actual p- value given as a own column. This is after all the main outcome-<br>-Table 3 and the related results is very unclear and unconvincing.<br>-In general , in the result section, the most important results should be presented in a clear and understandable fashion and supplemented by the tables. In the presented paper, the tables are explained.<br>- table 4 is good in itself, but the explanation in the text is confusing and too long.<br>14: the article´s readability would benefit considerably from proof reading |

**VERSION 2 – AUTHOR RESPONSE**

| **Reviewer: 2**<br>Dr. Risa Anna Margareth Lonnee-Hoffman , NTNU | |
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| **Comments to the Author:** | **Authors' Responses:** |
| Dear Authors!<br>The manuscript is much improved, thank you for that. However, there are still some issues. | We want to thank the reviewer for further comments to improve our manuscript. |

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| 1. Most importantly, I cannot agree on your aim/objective for the study, given the available outcome. Your outcomes are self- reported STIs and possible symptoms of STIs. Therefore, this should be stated consistently without leading to misunderstandings. | Thank you for bringing this to our attention. We made edits to consistently clarify the outcomes as **self-reported** STI and symptoms. |
| 2. See above. Therefore both objectives and results should be changed accordingly. | We made edits to clarify the outcomes as **self-reported** STI and symptoms in both our objectives and results as well. |
| 3. The design is not possible to change. Therefore you should re-formulate the research question. | We agree that the repeated cross-sectional nature of the study design is inherent therefore not possible to change. The research question focuses on describing the changes of prevalence of self-reported STI and its associations with demographic factors. |
| 4. The inclusion criteria for the selected cohort are still not described, neither is the method of data collection described. | We revised the section of samples and added more details as follow to further explain the inclusion criteria and elaborated Figure 1 on the selected cohort. We also added the data collection method descriptions.<br><br>“Both survey samples were systematically stratified in multiple stages by using the primary sampling units based on the size of rural villages and urban census blocks, and the randomly selected households within each cluster were chosen for interviews. A detailed sample design is described in the NFHS report. [26,27] As shown in Figure 1, the datasets had 39,257 and 63,696 matched couples in a household for NFHS-3, 2006 and NFHS-4, 2016 survey wave, respectively; when both waves were combined, there were 102,953 couples identified. Then, a sample of 102,690 couples from two survey waves were analyzed for self-reported STI analyses after excluding couples with unknown and missing self-reported STI status. For the multivariate analyses, a sample of 97,288 couples were analyzed after excluding couples with missing covariates. After accounting for unknown and missing variables, among those with at least one self-reported STI or symptoms, we identified 5,017 husbands and 10,631 wives to analyze the outcomes for individuals who sought treatment or advice for STI or its symptoms.” |
| 5. For the original data collection- was there no consent required? And, were the partners aware of each others answers? | We made the following text to explain the data collection process, including consent and private interview setting.<br><br>“Informed consent for participation in the survey were obtained for all respondents prior to each interview. Interviewers were trained to interview the respondent alone to establish privacy—without presence of other eligible respondents in the household.” |

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| 6. The outcome measure of self reported STI and STI symptoms is appropriate. However, it is not quite clear and convincing why an artificial outcome needs to be constructed - the couples STI status. This outcome has not been measured directly and should be not used as a hard outcome in tables in line with collected data. Either a more convincing explanation of this construction should be given in the method section or it could be mentioned in the discussion as possible interpretation of the results. | STI among any partner in a marriage affects the couple's sexual health and intimate partner relationship. Therefore, it is necessary to study couple's STI status based on either partner or both infected. Prior literature defined couple's STI as either partner or both infected, which has been used in study sexual health among married couples in India. Therefore, we revised the text and added one new citation:<br><br>"Because STI among any partner in a marriage affects the couple's sexual health and family relationship, we followed prior method [28] and grouped the self-reported STI prevalence of at least one of the married couples as a single dichotomous variable to code as the primary self-reported STI outcome of a couple." |
| The casts should be explained shortly in the method section, as this is not commonly known and one wonders, if there could be a more culturally sensitive term than "backward class". | We added a short description of caste system and its negative impact in the Method section. |
| The questions are not quite clear. Only when looking at the results, it becomes more clear, that seperate questions are asked. Was there a separate question on "any STI symptoms" or is this a constructed variable? | The outcome for any STI symptom was coded for this study. We added more details to describe how each outcome was categorized. |

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| 9 and 10. Some of this is already mentioned. The results should be still more clearly presented.<br>- Nearly 50% more women have a higher education in 2016 compared to 2006, although employment is much less. this should be mentioned when presenting the results. | We agree with the reviewer and have tested for the differences of these demographics. We added the chi-squares/t-statistics and p-values to Table 1. We described the significant differences, especially for education levels and employment, from 2006 to 2016. "With exception to religion, there were significant differences in socio demographics (mean age, education, employment, caste, family wealth, and residence) of married women and men from 2006 to 2016. Compared to 2006, more women had higher education in 2016; for instance, only 6% of married women reported having college or higher education in 2006, and for 2016, about 10% of married women reported having education at college or above ($p<0.0001$). Wife's employment rate has significantly decreased over 10 years from 38% to 25% ($p<0.0001$). It should also be noted that similar directionality has been observed among married men: higher education has significantly increased, while employment has also significantly decreased from 97% in 2006 to 92% in 2016 ($p<0.0001$)." |
| SE is not that interesting, it could be in brackets , not an own column. | Thank you for your feedback on the readability of tables. We put SE into brackets. |
| Rather a statistical difference could be considered to be presented. Further, in the discussion this should mentioned,and explanations offered- are different populations selected, has the social pattern changed...? | In the Discussion section, we provided explanations on differences of socio demographics from 2006 to 2016, which details 'Right to Education Act,' and "jobless growth" in India. |
| - Table 2: consider to have the year as column, the variables as rows. | We agreed with the reviewer's suggestion and switched the column and row accordingly. |
| Recommend to drop "couples". | Couple's STI status based on either partner or both infected outcomes have been studied in existing literature. We believe that this couple's self-reported STI outcomes will help guide ongoing discussion around how marriage affects the couple's sexual health and intimate partner relationship. |
| It would be easier to read if the Chi - square is dropped and rather the actual p- value given as a own column. This is after all the main outcome- | Thank you for your feedback. We decided to keep the Chi-squares in Table 2 to show the magnitude of the association. We revised the table to show p-value in another column. |
| -Table 3 and the related results is very unclear and unconvincing.<br>-In general , in the result section, the most important results should be presented in a clear and understandable fashion and supplemented by the tables. In the presented paper, the tables are explained. | We revised the result section to present in a clear and concise manner. |

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| - table 4 is good in itself, but the explanation in the text is confusing and too long. | As mentioned above, we revised the result section to present in a clear and concise manner. We hope this revision further improves the readability. |
| 14: the article´s readability would benefit considerably from proof reading | Thank you for the feedback. We have proofread the manuscript again and made appropriate edits. |